Remarks

Reconsideration of this Application and entry of the Amendment is respectfully requested.

Claims 1 and 41 are sought to be amended. Support for the amendments can be found, *inter alia*, in paragraph 0027 of the captioned application, and throughout the specification and claims as originally filed. It is believed that these amendments will put the case in condition for allowance. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Upon entry of the foregoing amendments, claims 1-41 are pending in the application, with 1, 9, 17, 23-25 and 29-41 being the independent claims. Claims 10-40 have been withdrawn from further consideration as being drawn to non-elected inventions. Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objection to the Title

Applicants thank the Examiner for withdrawing the objection to the title in view of Applicants' amendment.

Objection to the Claims

Applicants' thank the Examiner for withdrawing the objection concerning the syntax of claim 8.

Rejections under 35 U.S.C. § 112, First Paragraph

The rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, has been maintained. (Paper No. 17, page 2.) The Examiner alleges "that undue experimentation is required to practice the invention as claimed." *Id.* Applicants respectfully traverse this rejection.

The test of enablement is whether one skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Undue experimentation is not required to practice Applicants' invention.

Factors that may be considered in determining whether experimentation is "undue" are set forth in *Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404, and include, but are not limited to: breadth of the claims; nature of the invention; state of the prior art; level of one of ordinary skill; level of predictability in the art; amount of direction provided by the inventor; existence of working examples; and quantity of experimentation needed to make or use the invention.

In particular, the Examiner asserted that :

> The breadth of the claims is excessive with regard to Applicants claiming methods of identifying agents which can treat any neurodegenerative diseases associated with amyloid aggregation or neuronal cell death. Applicants have only provided guidance and working examples of how to identify agents which mediate CCE in SY5Y cells as it pertains to Alzheimer's plaques. It is not predictable that diseases other than Alzheimer's could be treated, nor is it even predictable that Alzheimer's, itself, could be treated since the specification only discloses in vitro assays to measure CCE.

(Paper No. 17, page 3.) Applicants respectfully disagree.

Applicants respectfully submit that numerous errors were made in formulating the rejection under 35 U.S.C. § 112, first paragraph, as set forth in the points below:

1. The claims being rejected are drawn to methods of identifying agents, not the agents themselves;

2. The claims at issue are not "reach through" claims;

3. Applicants are not required to disclose or provide working examples of *all* neurodegenerative diseases that an agent might be capable of treating in order to enable the claims.

The specification and the knowledge in the art as of the priority date provide sufficient information and guidance such that one of skill in the art can practice the full scope of the invention without undue experimentation. For example, the specification provides non-limiting examples of assays and techniques that can be used for measuring CCE. (Specification Paragraphs 0028-29.) Non-limiting examples of cells that can be used to screen for compounds that potentiate CCE are provided in Paragraph 0031 of the specification, and non-limiting examples of neurodegenerative disease-linked mutations are provided in Paragraphs 0032-34. Furthermore, contrary to the Examiner's statement that only SY5Y cells were used in the working example (Paper No. 17, page 3), other cell types were used as well, including CHO cells, 293 cells, and cultured primary neurons derived from transgenic mice expressing wild-type or mutant forms of human PS genes. *See e.g.*, Specification Paragraphs 0075, 0078, 0080, 0085, 0089 and 0090. Also, Paragraph 0032 of the specification as filed provides numerous non-limiting examples of specific neurodegenerative diseases to be treated by compounds identified using the claimed method. All of this information provides one of skill in the art with

sufficient guidance to practice the method of claims 1 and 41, and those claims dependent thereon.

As set forth in the second point above, the claims are not "reach-through" claims. The Examiner alleges that, because claims 1-9 and 41 "are 'reach-through' claims . . . Applicants['] claims do need to be enabled for compounds which treat the claimed neurodegenerative diseases." (Paper No. 17, page 3.) However, the Examiner appears to have mischaracterized Applicants' claims. Typical "reach-through" claims are, for example, claims to compounds generated by a screening method rather than claims directed to the screening method itself. Such claims may raise issues under 35 U.S.C. § 112, first paragraph, because they may claim compounds that are not yet known. In the present case, however, claims 1-9 and 41 are effectively drawn to a screening method, not to the compounds obtained by that method. Therefore, the Examiner's concerns about "reach-through" claims are unfounded.

While some of the screened compounds are intended to be used to treat a neurodegenerative disease, that has no bearing on the scope of Applicants' method claims. The Examiner contends that "[i]f Applicants do not intend for the identified compounds to treat neurodegenerative diseases, then the claims should not recite this limitation and should simply be drawn to a screening method." (Paper No. 17, page 3.) Applicants reiterate that the claims *are* drawn to a method. The fact that the claims recite a method of identifying an agent capable of treating a neurodegenerative disease characterized by symptoms comprising amyloid aggregation or neuronal cell death does not alter the fact that the claims are directed to a method. Moreover, the Examiner's allegation that it is not "even predictable that Alzheimer's, itself, could be treated since

the specification only discloses *in vitro* assays to measure CCE" (Paper No. 17, page 3), blurs the distinction between a method of identifying an agent capable of treating a neurodegenerative disease and actual treatment of a neurodegenerative disease using an agent identified by the method. Even if the identified agent is ultimately used *in vivo*, the CCE measurement and identification of the agent could still be performed *in vitro*.

The Examiner further alleges that "Applicants have not provided a nexus that the identification of compounds which are active in vitro is indicative of an in vivo treatment." (Paper No. 17, page 3.) Contrary to this assertion, Applicants have provided such a nexus. For example, the specification as filed sets forth that FAD mutations in PS1 or PS2 give rise to an increased production of Aβ42 "*in AD patients . . . as well as transfected cell lines and transgenic animals expressing FAD mutant forms of PS1 or PS2*." (Specification Paragraph 0003 (citations omitted) (emphasis added).) Furthermore, as stated in Paragraphs 0005 and 0075 of the specification, "[t]he Aβ42-promoting effect of FAD mutant presenilins does not appear to be cell-type specific." This information indicates that *in vitro* and *in vivo* systems show the same phenotypic response to FAD mutations in PS1 and PS2, and that an *in vitro* system can therefore act as a model for *in vivo* systems. In any event, even if treatment were a concern, the Examiner is reminded that, to obtain a patent, Applicants are not required to perform the *in vivo* testing of efficacy and safety that is required, for example, to obtain FDA approval for a drug treatment. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995).

As set forth in the third point above, Applicants are not required to disclose or provide working examples of all embodiments of their invention. The Examiner alleges

that "Applicants have still not enabled the full scope of the claims with regard to identifying agents capable of treating all neurodegenerative diseases 'associated with neuronal cell death,'" and that "the specification does not provide any guidance or working examples of the effect of measuring CCE on any other neurodegenerative diseases other than Alzheimer's." (Paper No. 17, pages 2-3.) Applicants respectfully disagree.

"It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art" *See, e.g., In re Vaeck*, 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991) (citing *In re Angstadt*, 537 F.3s 498, 502-03, 190 U.S.P.Q. 214, 218 (CCPA 1976)). Furthermore, the specification *does* provide guidance regarding diseases other than Alzheimer's disease. For example, as described *supra*, Paragraph 0032 of the specification provides numerous non-limiting examples of specific neurodegenerative diseases that could be treated by compounds identified using the claimed method. Also, Paragraph 0099 of the specification discusses the contribution of CCE dysregulation in spinocerebellar ataxia type 1. In any event, as noted previously, the invention is drawn to a *method* of "identifying an agent," not the agent itself; therefore, this aspect of the rejection is incorrect. Applicants need not enable every neurodegenerative disease or every agent that might be discovered by the assay.

Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-9 and 41 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. (Paper No. 17, page 3.) In particular, the Examiner alleges that he "cannot find support for methods of screening compounds which are able to treat diseases associated with neuronal cell death." *Id.* Applicants respectfully traverse this rejection.

The specification as filed contains support for methods of screening compounds capable of treating diseases characterized by symptoms comprising amyloid aggregation or neuronal cell death. In particular, the specification indicates that CCE serves as a prominent Ca2+-refilling mechanism in neurons, and that changes in CCE influence apoptotic cell death. (Specification Paragraph 0007.) Also, Paragraph 0099 of the specification indicates that CCE may be an upstream event leading to increased vulnerability to apoptotic stimuli. Therefore, identifying compounds using the claimed method provides for identification of compounds capable of treating neurodegenerative diseases characterized by symptoms comprising amyloid aggregation or neuronal cell death. The totality of the information provided would convey to one of skill in the art that Applicants had possession of the claimed invention. Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, first paragraph, as allegedly adding new matter have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

Rejections under 35 U.S.C. § 112, Second Paragraph

Applicants thank the Examiner for withdrawing the rejection of claims 1-9 and 41 under 35 U.S.C. § 112, second paragraph. (Paper No. 17, page 4.)

Claims 1-9 and 41 were rejected under 35 U.S.C. § 112, second paragraph, as "confusing since the metes and bounds of 'associated with' are not defined." (Paper No. 17, page 4.) Solely to facilitate prosecution, to provide clarification, and to make explicit that which was implicit, Applicants have amended claims 1 and 41 to replace the phrase "associated with" with "characterized by symptoms comprising." Accordingly, the Examiner's grounds of rejection of claims 1-9 and 41 under 35 U.S.C. § 112, second paragraph, have been rendered moot. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw this rejection.

Rejections under 35 U.S.C. § 102

The rejection of claim 1 has been maintained under 35 U.S.C. § 102 as allegedly being anticipated by Buxbaum *et al.* (U.S. Patent No. 5,538,983; hereinafter "the '983 patent") and by Berridge, *Biochem J.* 312: 1-11 (1995) (hereinafter "Berridge"). (Paper No. 17, page 4.) Applicants respectfully traverse this rejection.

According to the Examiner:

> [t]he fact that the agent identified is capable of treating a neurodegenerative disease is an intended use and does not have any patentable weight. One way to look at this is to consider two artisans side by side. One performing the present method and the other performing the method of Birnbaumer. Regardless of the intended use of the compounds identified by each of the artisans, both procedures would appear (and, i[n] fact, be) identical to the onlooker.

Id. Applicants respectfully disagree.

First, Applicants submit that the '983 patent does not anticipate the claimed invention because it does not teach assaying for CCE activity in cells treated with an agent, assaying for CCE activity in cells untreated with the agent, and comparing the CCE activities to determine whether the agent potentiates CCE activity in cells treated with the agent. Rather, the '983 patent describes "detecting alterations in the secretion of APP, and the production of Aβ." (The '983 patent, col. 2, lines 26-27.) Accordingly, the rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Second, Applicants maintain that, because Berridge does not describe identifying an agent capable of treating a neurodegenerative disease characterized by symptoms comprising amyloid aggregation or neuronal cell death, the document does not describe each and every limitation of Applicants' claimed invention. However, solely in a effort to facilitate prosecution, Applicants have amended claims 1 and 41 to recite a step (d): "testing said identified agent in animal studies." Accordingly, the rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The rejection of claims 1, 9, and 41 has been maintained under 35 U.S.C. § 102 as allegedly being anticipated by Birnbaumer *et al.* (U.S. Patent No. 5,932,417; hereinafter "the '417 patent"), for the same reasons set forth by the Examiner with respect to the '983 patent and Berridge. (Paper No. 17, page 4.) Applicants respectfully traverse this rejection.

Applicants maintain that, because the '417 patent does not describe identifying an agent capable of treating a neurodegenerative disease characterized by symptoms comprising amyloid aggregation or neuronal cell death, the document does not describe each and every limitation of Applicants' claimed invention. However, solely in a effort to facilitate prosecution, Applicants have amended claims 1 and 41 to recite a step (d): "testing said identified agent in animal studies." The '417 patent does not discuss testing in animal studies. Accordingly, the rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The rejection of claims 1, 9, and 41 has been maintained under 35 U.S.C. § 102 as allegedly being anticipated by Birnbaumer *et al.*, *Proc. Natl. Acad. Sci.* 93: 15195-15202 (1996) (hereinafter "Birnbaumer *et al.*"), for the same reasons set forth by the Examiner with respect to the '983 patent, Berridge, and the '417 patent. (Paper No. 17, page 4.) Applicants respectfully traverse this rejection.

As above, Applicants maintain that, because Birnbaumer *et al.* do not describe identifying an agent capable of treating a neurodegenerative disease characterized by symptoms comprising amyloid aggregation or neuronal cell death, the document does not describe each and every limitation of Applicants' claimed invention. However, solely in a effort to facilitate prosecution, Applicants have amended claims 1 and 41 to recite a step (d): "testing said identified agent in animal studies." Thus, Applicants have clarified that Birnbaumer *et al.* do not anticipate the claimed invention. Accordingly, the rejection has been overcome or otherwise rendered moot, and Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 103

Applicants thank the Examiner for withdrawing all of the rejections under 35 U.S.C. § 103.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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